NIH - CMRR 2003

Task-Oriented Exercise After Stroke:

Mechanisms of Neuromuscular Plasticity

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Stroke: A Major Public Health Issue

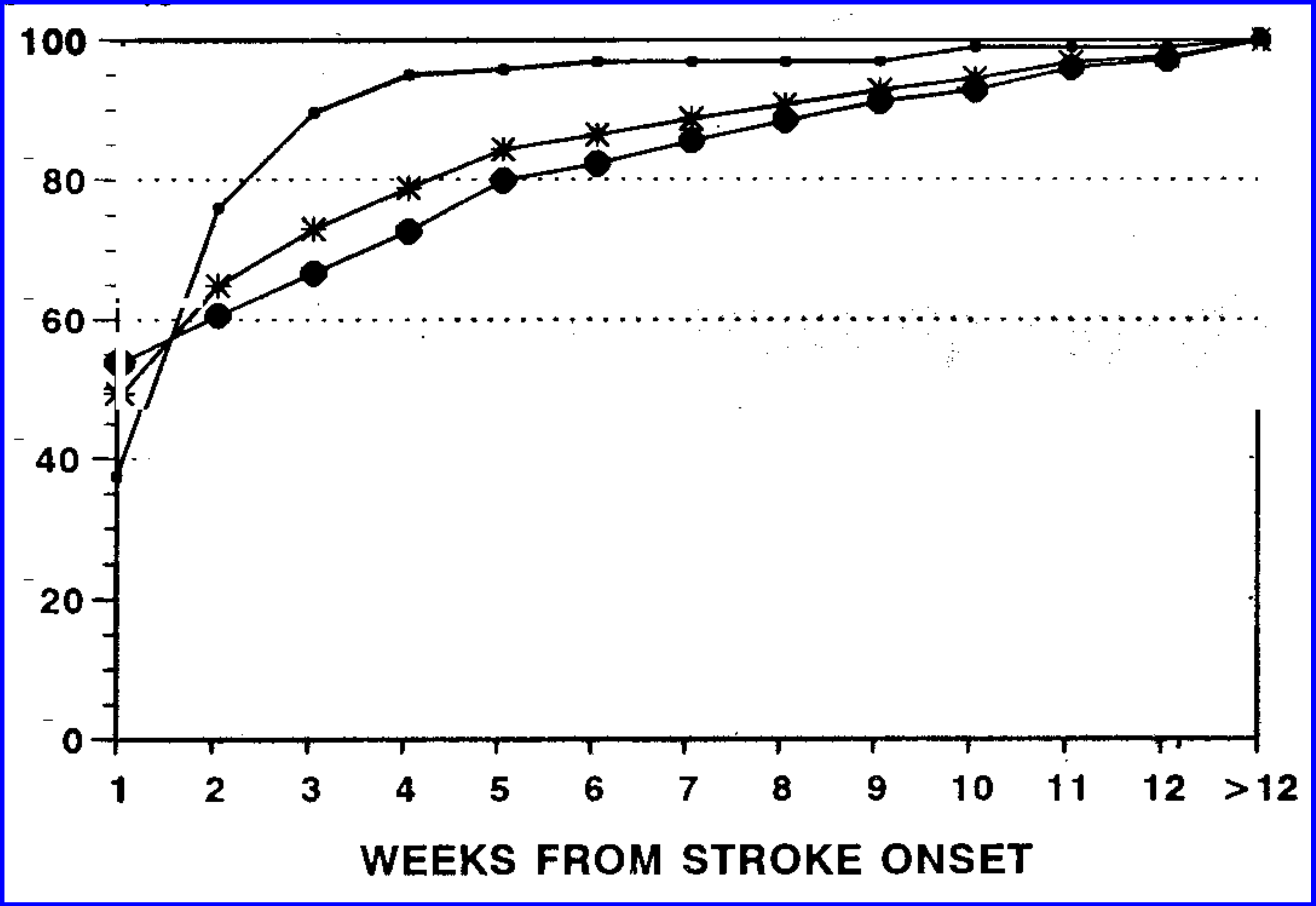
780,000 strokes/yr in U.S. Chronic deficits in 75%.

- **Conventional rehabilitation**- front loaded during the sub-acute recovery period (<3 months); emphasizes recovery of ADL function & prevention of complications.

- **Patients become physically inactive**, which compounds disability by physical deconditioning and learned non-use.

No evidence-based recommendations to promote regular exercise in stroke population.

Percent of stroke patients with stationary gait function and leg motor strength recovery during conventional rehabilitation



N=804

95% get no better after 11 weeks with routine care.

Jorgenson et al. Arch Phys Med Rehabil 1995

What may be deficient in conventional rehabilitation models ?

1. Is the exercise intensity enough?

- Typical 51 minute PT session, < 3 minutes at low aerobic intensity (>40% HRR)

McKay Lyons et al. 2002

2. Is repetition adequate?

- 20-30 minutes practice needed to produce short-term cortical motor adaptations in normal adults.

Classen 1998

3. Do we exploit the full time window for plasticity?

- Extends beyond 3-6 months

Liepert 2001

OUTLINE

I. What is biological basis for task-oriented exercise after stroke?

- Peripheral Mechanisms - cardiovascular deconditioning and muscle abnormalities contribute to disability.
- Central Neural Mechanisms – task repetition is critical for promoting motor learning by neural plasticity.

II. What is the evidence that task-oriented exercise can improve function and fitness in chronic stroke ?

How unfit are chronic stroke patients?

- **We tested fitness levels & energy demands of gait in 53 patients**
- **44 men, 9 women**
- **Mean Age 65 $\pm$ 8 years**
- **Mean 3 years post-stroke**
- **Hemiparetic gait, not wheelchair bound.**

ECONOMY OF GAIT

- Purpose - estimate the energy demands of hemiparetic gait.
- Protocol - Treadmill walk at 75% of self-selected floor-walk pace, no incline for 9 minutes.
- Rate of $V0_2$ calculated from final 3 minutes at steady state oxygen kinetics.

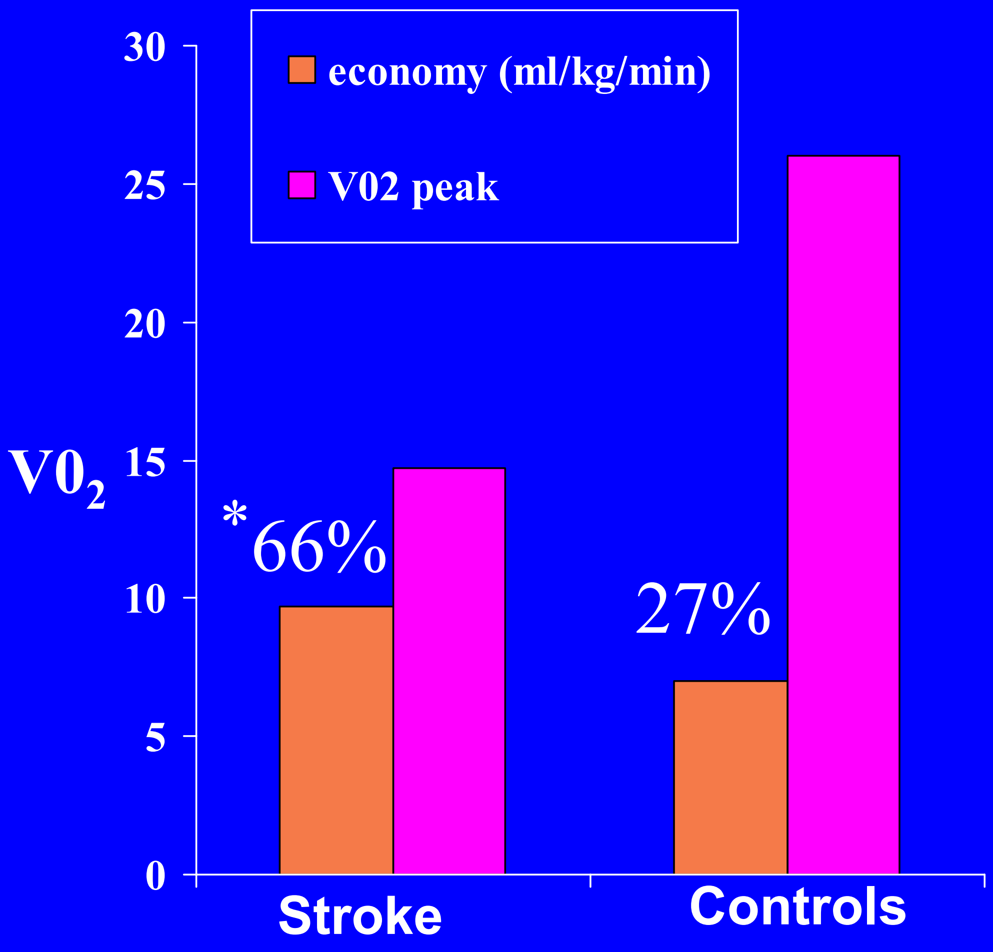
Chronic stroke patients have diminished fitness reserve

Low Peak Fitness Levels

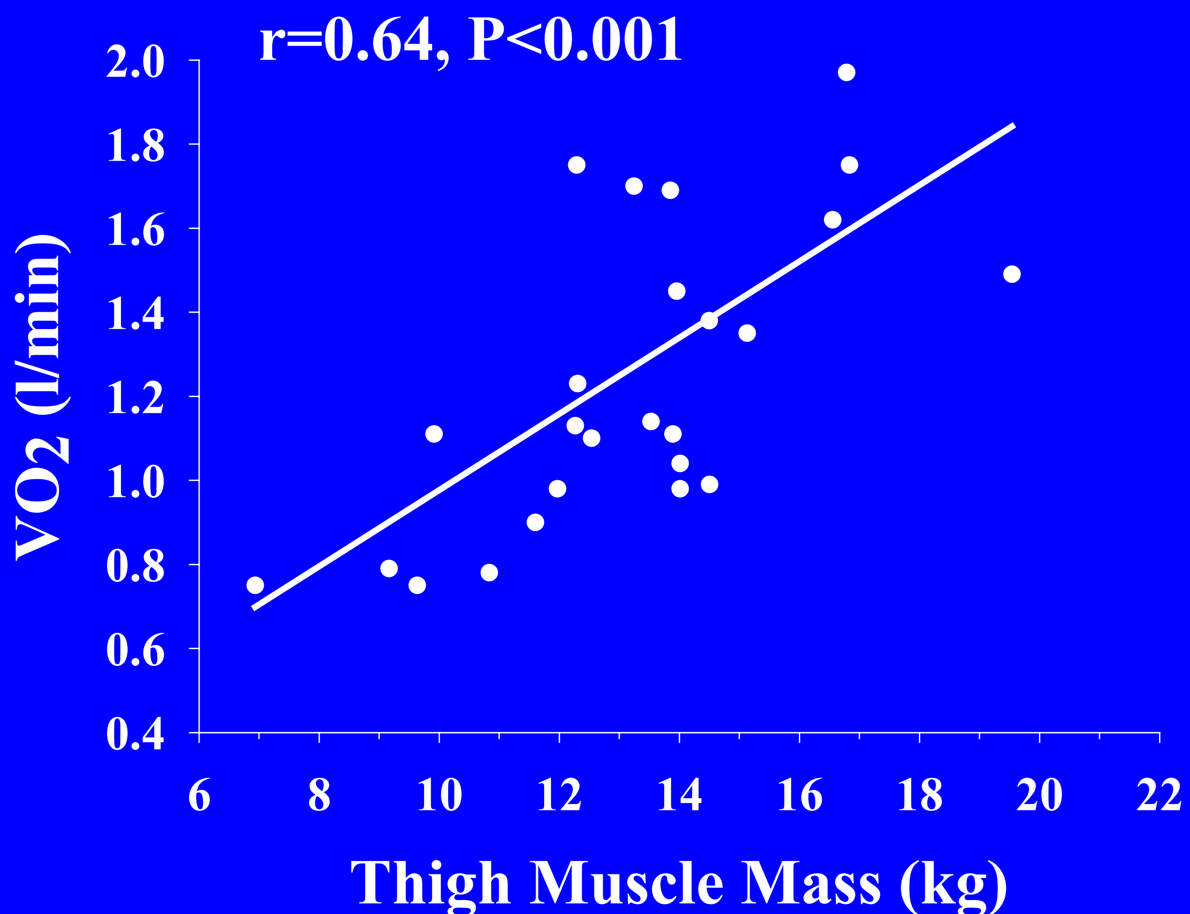
- $V0_2$ Peak = 14.7 $\pm$ 4 ml/kg/min;
- 44% below sedentary controls.

Poor Economy of Gait:

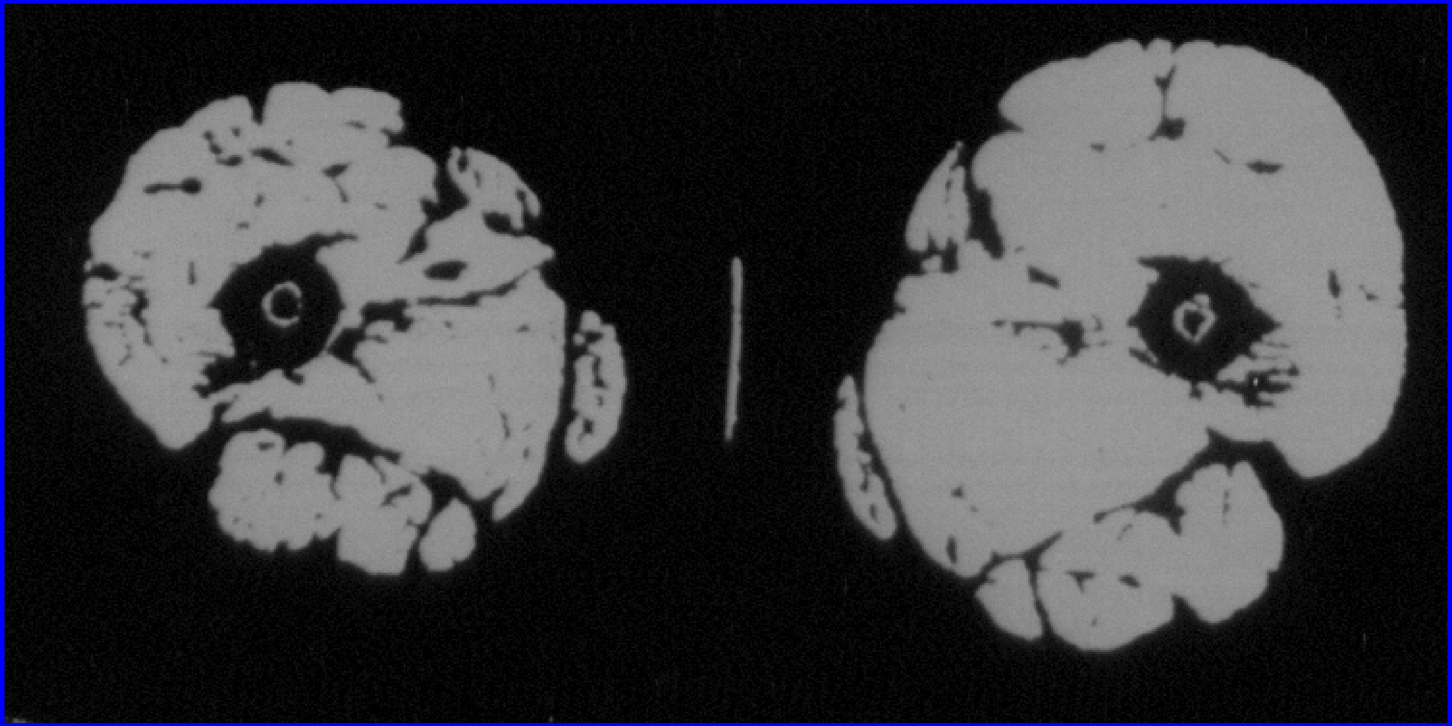
- Mean rate $V0_2$ 9.7 $\pm$ 2 ml/kg/min



Relationship of peak VO_2 to thigh muscle mass (DXA)



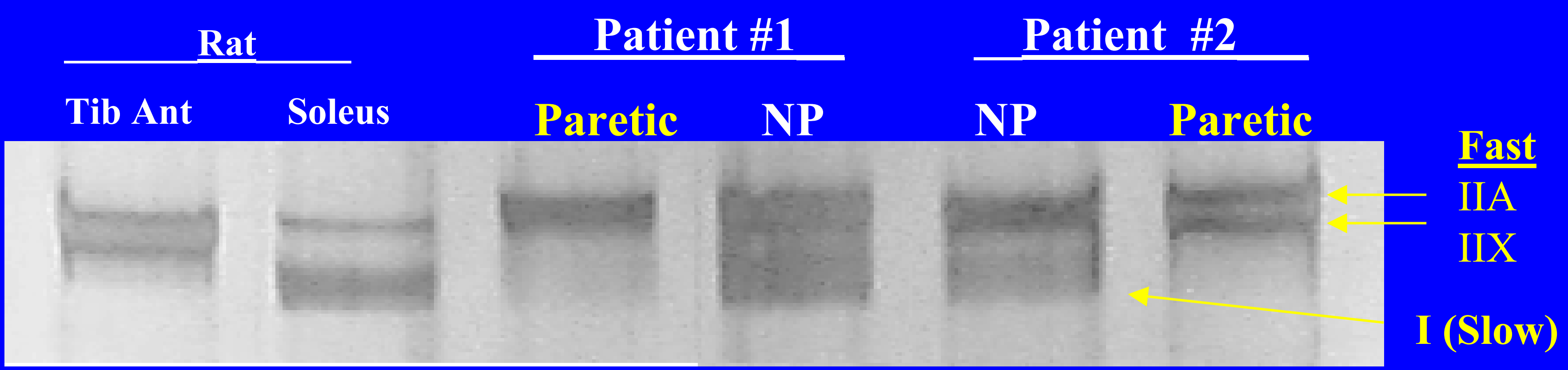
CT Scan of the Mid-Thigh Cross-Sectional Muscle Area in a Stroke Patient



Muscle area is 20% lower in hemiparetic thigh (N=30, P<.001).

Changes in Paretic Leg
Skeletal Muscle Phenotype after Stroke

Myosin Heavy Chain Profile



Increased fast MHC isoforms in paretic leg vastus lateralis.

Paretic leg = *67%   Unaffected leg = 51%   (*p<.001, N=15)

Fast MHC is prone to fatigue, and insulin resistant.

DeDeyne, submitted

Rationale for exercise after stroke:

- Physical deconditioning threatens the capacity of stroke patients to meet the high energy demands of hemiparetic gait.
- Patients with the most muscular wasting (sarcopenia) in their thighs are at greatest risk for functional aerobic impairment.
- Changes in muscle may contribute to motor weakness, fatigue, and increased cardiovascular disease risk by promoting insulin resistance.

Biomechanical basis for treadmill to promote locomotor re-learning

TM Improves Gait Symmetry

- 20% higher stance:swing ratio on P leg; 20% lower on NP leg.
- 30% improved symmetry of insole forces.
- 40% less cycle-cycle variability.

Harris-Love et al. J Neur Rehab Neural Rep 2001

Initial pilot and feasibility studies of treadmill (TM) training

HYPOTHESIS

6 months TM training will improve fitness and function in chronic hemiparetic stroke?

RESULTS

- Reduces energy demands of HP gait 16%
  Macko 1997
- Improves peak fitness 10% & work load 39%
  Macko 2001
- Improves floor walking velocity by 21%
  Silver 2000
- Increases P leg strength 50% & balance.
  Smith 1999, Smith 2000

Study Limitations

Non - controlled. No comparison to conventional care.

RANDOMIZED STUDY
Treadmill AEX vs Active Control

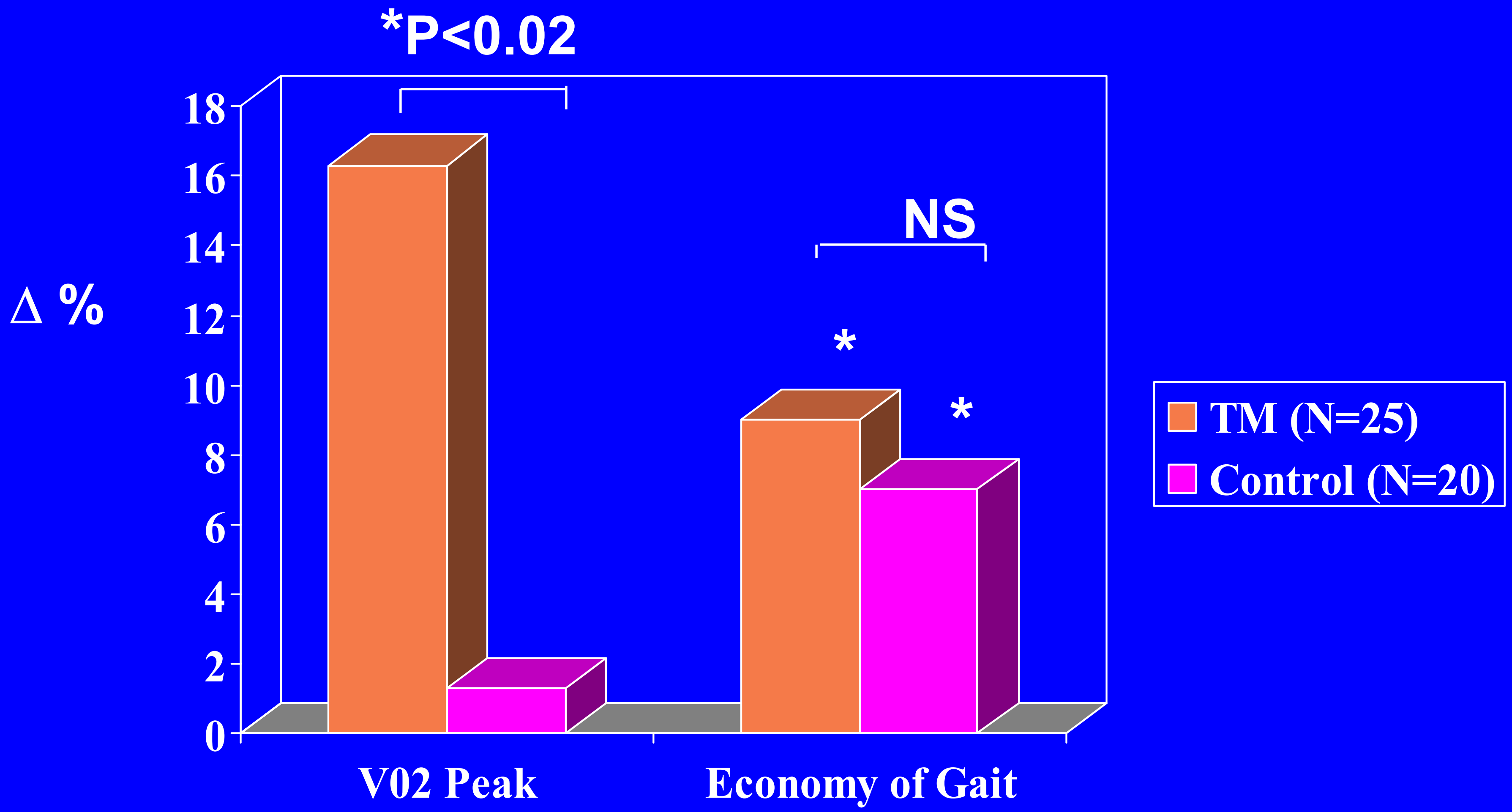
Purpose: Determine whether 6 months TM aerobic training (60 -70% HRR) improves fitness, economy of gait, and floor walking in chronic stroke patients, compared to controls receiving a dose-matched form of conventional care.

- **Active Controls: 45 minutes stretching exercises; 5 minutes warm-up of low intensity treadmill walking (30-40% HRR).**

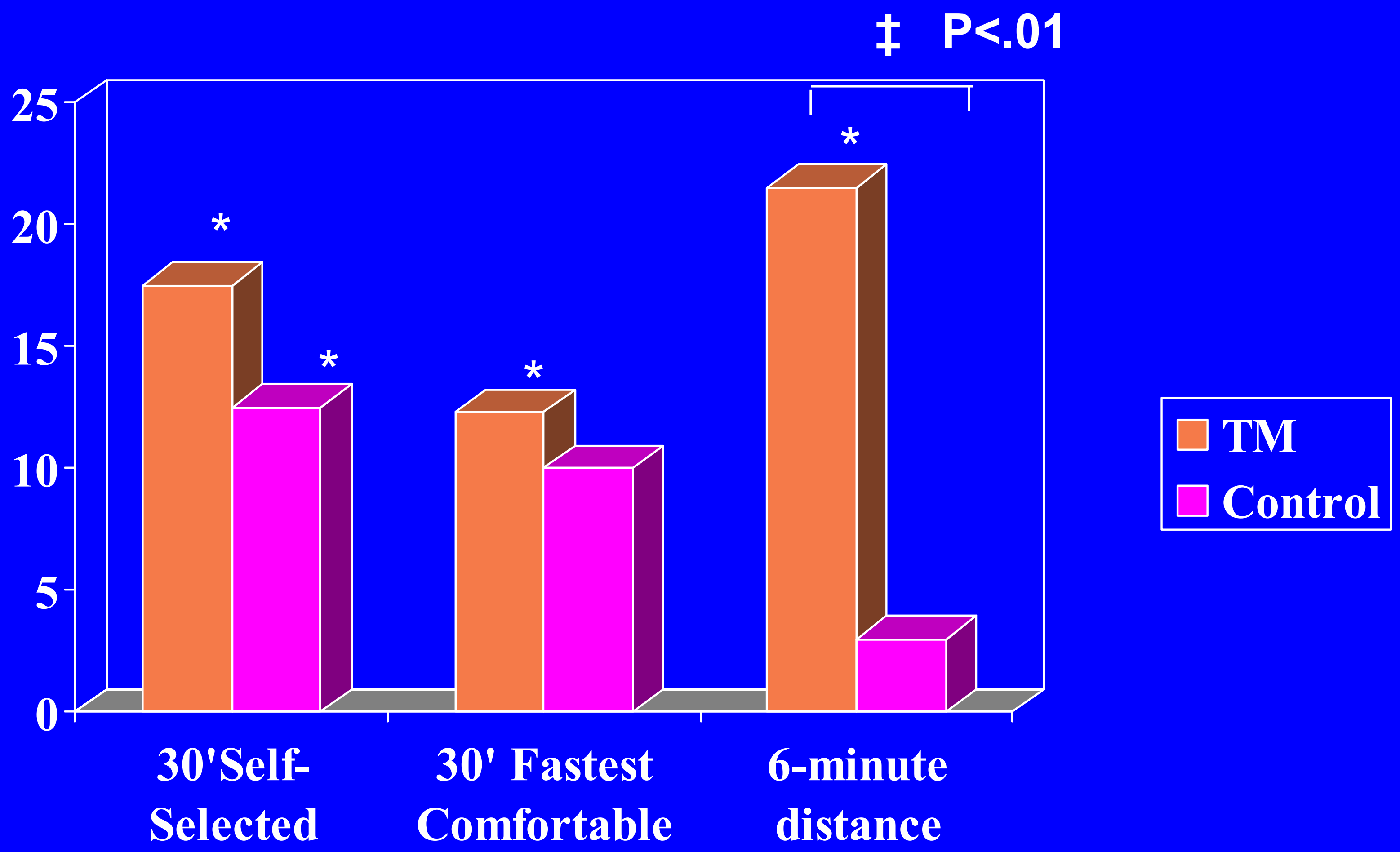
SUBJECTS: Clinical & Demographic Features

	TM	Control
◆ Males : Females	18 : 7	14 : 6
◆ Age (yrs)	65 $\pm$ 10	63 $\pm$ 8
◆ Hemisphere (R : L)	12 : 13	9 : 11
◆ Time since stroke (M)	32 $\pm$ 30	42 $\pm$ 65
◆ Assistive Device		
– None	9 (37.5%)	5 (24%)
– Single point cane	10 (37.5%)	11 (57%)
– Quad cane/walker	6 (25%)	4 (19%)
◆ Floor Walking Speed (range MPH)	1.4 $\pm$ 0.7 (0.25 - 2.7)	1.5 $\pm$ 0.7 (0.19 - 2.6)

RESULTS: Effects of Treadmill Training on Fitness after Stroke



Effects of Treadmill Training on Walking Performance



*P<.01 Within groups

CONCLUSIONS - Randomized Study

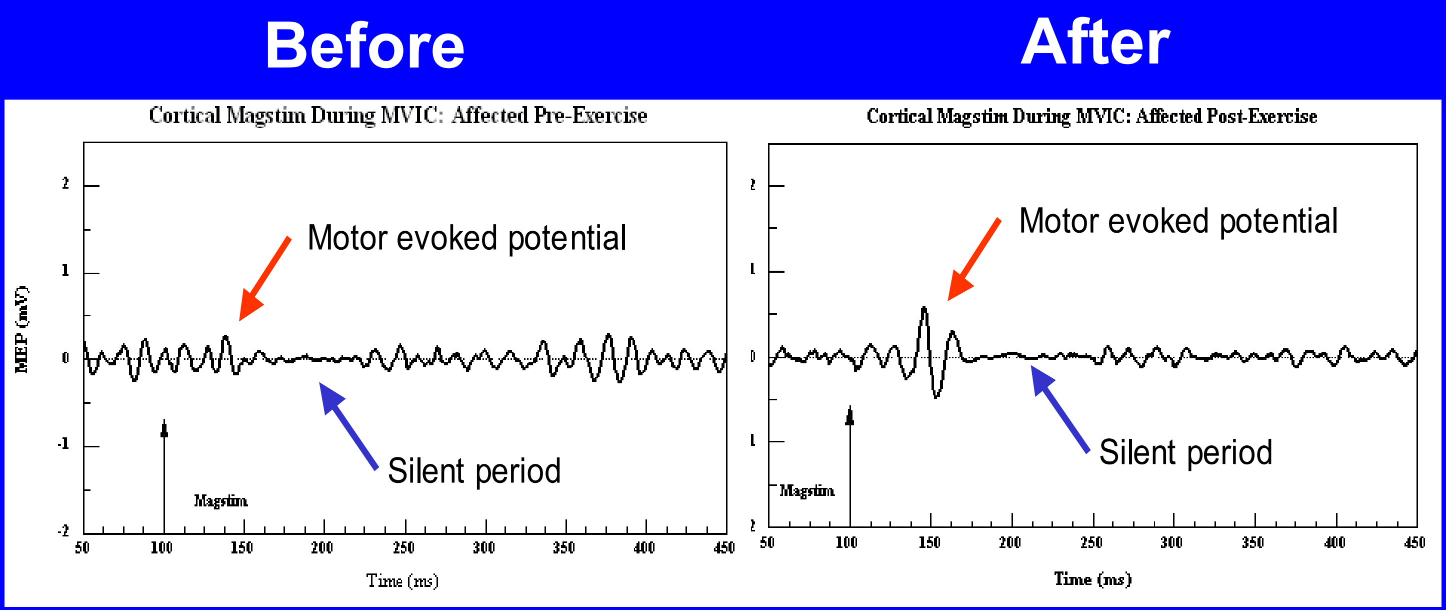
I. <u>Treadmill</u> & <u>stretching/low intensity walking</u> both improve economy of gait and 30’ floor walk velocity.

II. Only <u>TM aerobic training</u> improves cardiovascular metabolic fitness & 6 -minute floor walk performance.

<u>Biological Mechanisms ?</u>

- Studies investigating the hypothesis that TM exercise mediates central neuroplasticity are ongoing …..

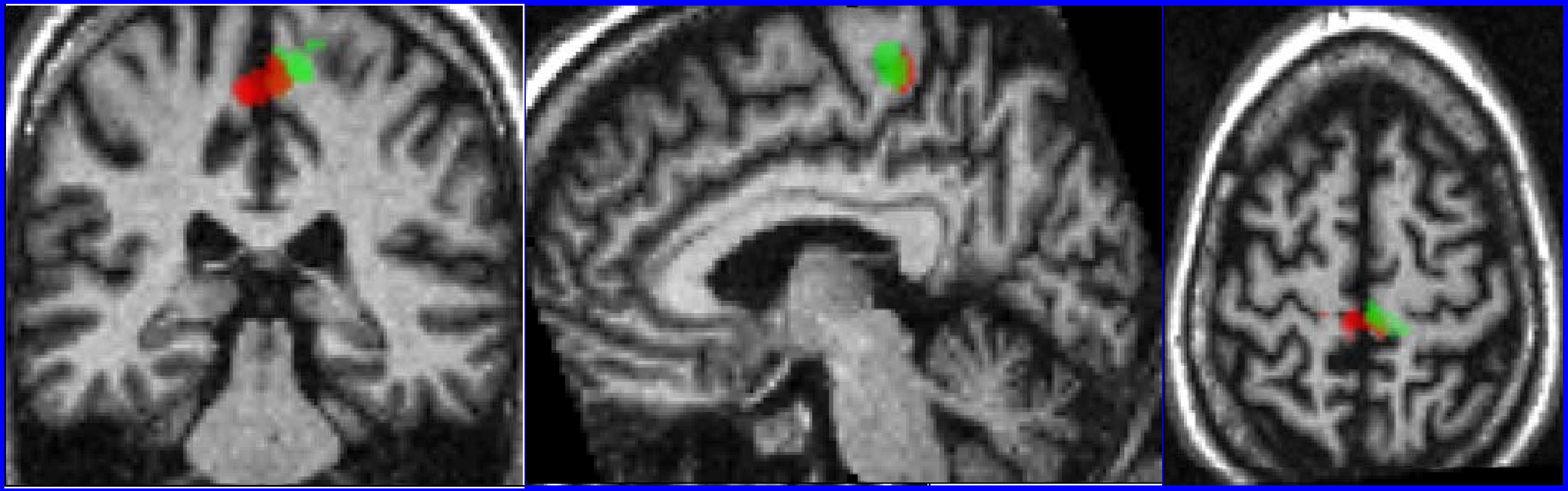
Transcranial Magnetic Stimulation (TMS) -Motor evoked potentials from paretic quadriceps before and after a single 20 minute treadmill session:



Trained Patients – Increased MEP amplitude paretic VL muscle.

Forrester et al. 2003 Submitted

BOLD fMRI
During Knee Movement in a Stroke Patient



Green - activation of motor cortex during movement of unaffected knee.

Red - activation of motor cortex during movement of the paretic knee.

A. Luft,, G Smith, L. Forrester, R Macko, A Goldberg, D. Hanley

Future Research:
Robotics assisted exercise rehabilitation

<u>MIT- ankle robotics module</u>

- **Impedance controlled**
- **6 degrees of freedom**
- **Programmable**
- **Evaluate applications in stroke and other neurological conditions**

<u>MIT Newman Lab</u>

Igo Krebs; Neville Hogan, Jason Wheeler.

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Experimental Design

Non-controlled study with measures of…

- **<u>Fitness</u> - $V0_2$ peak, economy of gait.**
- **<u>Functional Mobility</u> - Timed floor walks, Get-Up and Go, translational balance perturbation.**
- **<u>Strength</u>- Isokinetic dynamometry.**

….at baseline and after exercise training.